IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Allen, Keith D.	Examiner:	Wilson, Michael C.
Serial No.:	10/005,202	Group Art Unit:	1632
Filed:	12/04/2001	Docket No.:	R902/75658.023400
Title:	TRANSGENIC MICE CONTAINING KIR5.1 INWARDLY RECTIFYING POTASSIUM CHANNEL GENE DISRUPTIONS		

DECLARATION OF ROBERT DRISCOLL PURSUANT TO 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Robert Driscoll, residing at 23 Chicory Lane, San Carlos, CA 94070, hereby declare:

1. I am presently employed as Vice President of Intellectual Property & Legal Affairs at Assignee, Deltagen, Inc., in San Carlos, CA. I have also previously served as the Company's Senior Director of Intellectual Property, in which position I managed and oversaw the Company's intellectual property portfolio, including the Company's patent filings. I possess a Ph.D in Chemistry, received from the California Institute of Technology. I also possess a J.D., received from Loyola Law School, Los Angeles. I am a registered patent attorney (Reg. No. 47,536).

2. I am familiar with the above-cited application. I am familiar with the Office Action mailed April 20, 2005. I am aware that the Examiner has rejected the claims, in part, for allegedly failing to meet the utility requirement. I am also aware that the Applicant has argued that a commercial sale of a mouse with a disrupted Kir5.1 inwardly rectifying potassium channel allele within the scope of the claimed subject matter ("Kir5.1 gene knockout mouse") should satisfy the utility requirement.

3. In support of the Applicant's aforementioned argument, I hereby state that I have reviewed Deltagen's internal sales records regarding the Kir5.1 gene knockout mouse. According to these records, the Kir5.1 gene knockout mouse has been delivered to at least one (1) large pharmaceutical company. The contractual terms by which the mice were transferred prohibit Deltagen from identifying the name of this company. However, the company is ranked among the top 10 pharmaceutical companies worldwide (based on sales).

4. It is my understanding, based on communications with our pharmaceutical company customers, that transgenic knockout mice obtained from Deltagen are used for studying gene function and for human therapeutic drug development.

5. I further declare that all statements made herein of my own knowledge are true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application or any patent issuing thereon.

Robert Driscoll, Ph.D, Reg. No. 47,536

9 June 2005

Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Serial No.:	10/005,202	Group Art Unit:	1632
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Title:	TRANSGENIC MICE CONTAINING KIR5.1 INWARDLY RECTIFYING POTASSIUM CHANNEL GENE DISRUPTIONS		

DECLARATION OF JOHN BURKE PURSUANT TO 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, John E. Burke, residing at 16357 E. Berry Avenue, Centennial CO 80015, hereby declare:

1. I am currently, and have been since 1998, the Attorney of Record for the Applicant and Assignee, Deltagen, Inc. I am listed on the originally filed Power of Attorney for the present application. From December 1996 to December 1999, I was Of Counsel with the law firm of Pillsbury Madison & Sutro (currently Pillsbury Winthrop) where I represented Deltagen with respect to intellectual property matters, including patent matters relating to their transgenic mouse program. From December 1999 until December 2001, I served as Deltagen's Vice President of Intellectual Property, where I supervised Deltagen's internal patent department. All of the applications, including the present application, covering the 750 lines of mice in DeltaBase were drafted by Deltagen's patent department. From December 2001 until April 2003, I served as Deltagen's Senior Vice President and General Counsel. From April 2003 through April 2005, I was a partner with the Denver office of Merchant & Gould, where I continued to represent Deltagen with regard to intellectual matters, including patent matters. I am presently employed as a Shareholder with the Denver office of the law firm of Greenberg Traurig, where I am responsible for prosecution of Deltagens's patent portfolio relating to their transgenic mice program, including the present application.

2. I am familiar with the present application. I am familiar with the Office Action mailed April 20, 2005. I am aware that the Examiner has rejected the claims, in part, for allegedly failing to meet the utility and enablement requirements. I am aware that the Examiner argues on pages 7-8 of the Office Action that background and genetic factors have an effect on phenotypes such as the startle response.

3. I hereby declare that, as evidenced by the attached Exhibit, the subject matter of the present application, Kir5.1 inwardly rectifying potassium channel gene knockout mice (Kir5.1 gene knockout mice), were compared with control mice of identical background.

4. I hereby declare that the claimed Kir5.1 gene knockout mouse has been extensively analyzed using the tests set forth in the Examples. This data has been incorporated into Deltagen's commercial database product, DeltaBase. This database has been subscribed to by at least three of the world's largest pharmaceutical companies, Merck, Pfizer and GSK.

5. I hereby declare that I have accessed Deltagen's internal web-based DeltaBase database to review the data derived from analyses of the claimed mice. I hereby declare that the attached Exhibit contains four (4) pages, each representing a screen printout from DeltaBase. The first page is the Behavior Summary page summarizing changes relating to genotype associated with Gene 902, as prepared by Deltagen's pathology group. As noted at the top of the page, Gene 902 corresponds to the Kir5.1 gene. As noted, the homozygous mice were significantly different in their startle response relative to wild-type controls. The page further notes that for the behavioral tests, 9 homozygous mutant males were compared with 10 wild-type controls males. The page further describes how 129/OlaHsd x C57BL/6 F2N1 mice were produced. The table on the right side of the page provides the background of each of the homozygous (-/-) and wild-type control mice (+/+) used in the comparative tests. As is shown in the table, the transgenic mice (-/-) and control mice (+/+) are of identical F2N1 background (129/OlaHsd x C57BL/6).

6. The second and third pages represent the "left" and "right" sides of a webpage showing a portion of raw data derived from the comparative startle/PPI tests for Gene 902. The gene number, 902, is indicated in column 1. The ES cell line is indicated in column 2. As can be seen, each mouse was derived from the same ES cell line, 1006. Columns 3 and 4 indicate the

generation and background. As can be seen, each mouse is of identical background, F2N1. As can also be seen, each mouse tested is of approximately the same age and gender. Column 35 (page 3) shows the date on which the data was recorded. All of the data corresponding to the F2N1 mice was entered prior to the filing date of the present application.

7. The fourth page of the Exhibit shows the statistical values for the startle test for Gene 902. As shown, the data derived was statistically significant.

8. In summary, the attached Exhibits show that the transgenic mice were compared with control mice of identical background. The phenotypes were based on a comparison with age, gender and strain matched control mice.

9. I further declare that all statements made herein of my own knowledge are true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application or any patent issuing thereon.

JER

John E. Burke, Reg. No. 35,836

7-6-05

Date

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Release: All
Program: All
Family: All
Subfamily: All
Show: by G

957 genes fou

9 Channel
10 Channel
11 Channel
12 Channel
13 Channel
15 Protease
16 Protease Ir
17 GPCR
20 GPCR
21 Carbohydr
24 Carbohydr
25 Carbohydr
28 Carbohydr
31 Carbohydr
37 Growth Fa
41 GPCR
42 GPCR
43 GPCR

Phenotypic Release Summary
Phenotypic Data Statistics
Target Research Database
SUMMARY
ANNOTATIONS
MOLECULAR BI
EXPRESSION AN
PATHOLOGY
CLINICAL FINDI
BEHAVIOR
FERTILITY/DEV
NEUROSCIENCE

Gene: 902 Name: Kcnj16 Family: Channel Subfamily: Potassium Alternative Names

Nucleotide Sequence Accession: AB016197 GI: 3953532 External Links: Select External Database

Last Modified By:Siebel, Sara
Last Modified On:11/5/2001 11:12:13 AM

Gene 902
Behavior

Changes related to genotype:

- Homozygous mutants displayed increased startle responses across all stimulus levels in the Startle/PPI test.

Homozygous mutant and wild-type control mice were evaluated for phenotypic changes by testing on six behavioral tasks: Open field test, Tail suspension test, Rotarod test, Hot plate test, Startle/PPI, and Metrazol test.

Mouse ID numbers are as follows:

9 homozygous mutant males (117341, 127734, 127771, 135164, 111590, 117319, 117320, 111592, 135184)
10 wild-type control males (138630, 127778, 117321, 117348, 117338, 135163, 111564, 111565, 127772, 135180)

ES cells derived from the 129/OlaHsd mouse substrain were used to generate chimeric mice. F1 mice were generated by breeding with C57BL/6 females. The resultant F1N0 heterozygotes were backcrossed to C57BL/6 mice to generate F1N1 heterozygotes. F2N1 homozygous mutant mice were produced by intercrossing F1N1 heterozygous males and females.

Behavior Findings:
When compared to age- and gender-matched wild-type control mice, homozygous mutant mice were significantly different in their startle response on the Startle/PPI test. Mutants displayed higher startle responses than their wildtype littermates. This may indicate a propensity for increased fear.

Mice

#	Sex	Genotype	F Gen.	N Gen.	Age	Validity	Release
111590	Male	-/-	2	1	68	V	T
111590	Male	-/-	2	1	75	V	T
111592	Male	-/-	2	1	68	V	T
111592	Male	-/-	2	1	75	V	T
117319	Male	-/-	2	1	68	V	T
117319	Male	-/-	2	1	85	V	T
117320	Male	-/-	2	1	68	V	T
117320	Male	-/-	2	1	85	V	T
117341	Male	-/-	2	1	68	V	T
117341	Male	-/-	2	1	85	V	T
127734	Male	-/-	2	1	69	V	T
127734	Male	-/-	2	1	84	V	T
127771	Male	-/-	2	1	68	V	T
127771	Male	-/-	2	1	83	V	T
135164	Male	-/-	2	1	71	V	T
135184	Male	-/-	2	1	70	V	T
135184	Male	-/-	2	1	79	V	T
111564	Male	+/+	2	1	68	V	T
111564	Male	+/+	2	1	75	V	T
111565	Male	+/+	2	1	68	V	T
111565	Male	+/+	2	1	75	V	T
117321	Male	+/+	2	1	68	V	T
117321	Male	+/+	2	1	85	V	T
117338	Male	+/+	2	1	68	V	T
117338	Male	+/+	2	1	85	V	T
117348	Male	+/+	2	1	68	V	T
117348	Male	+/+	2	1	85	V	T
127772	Male	+/+	2	1	68	V	T
127772	Male	+/+	2	1	83	V	T
127778	Male	+/+	2	1	69	V	T
127778	Male	+/+	2	1	84	V	T
135163	Male	+/+	2	1	71	V	T
135163	Male	+/+	2	1	80	V	T
135180	Male	+/+	2	1	70	V	T
135180	Male	+/+	2	1	79	V	T
138630	Male	+/+	2	1	70	V	T
138630	Male	+/+	2	1	84	V	T

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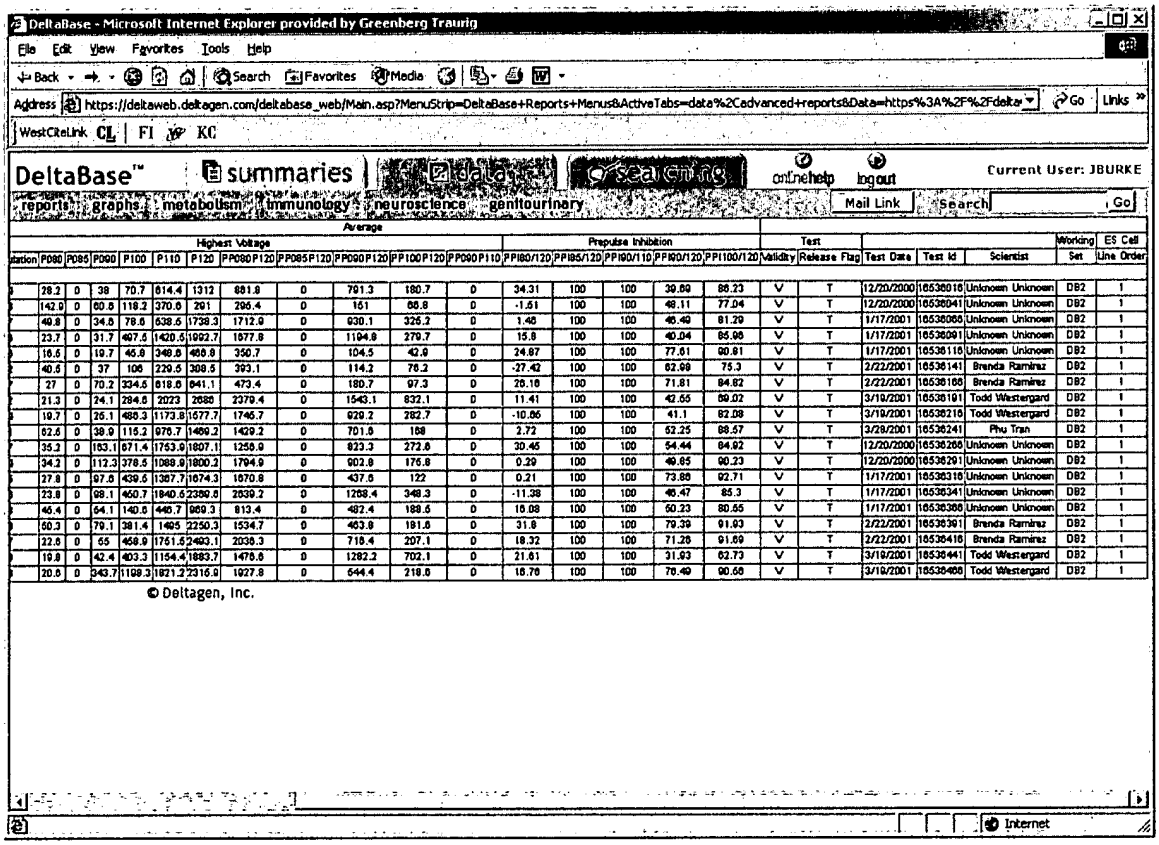
									Average																	
	ES Cell								Highest Voltage													Prepulse Inhibition				
Gene	Line	F #	N #	Genotype	Gender	Age at Test (days)	Mouse	Chamber	No Stimulation	P080	P085	P090	P100	P110	P120	PP080P120	PP085P120	PP090P120	PP100P120	PP090P110	PPI80/120	PPI85/120	PPI90/110	PPI90/120	PPI100/12
902	1006	2	1	+/+	Male	73	111564	1	42.4	28.2	0	38	70.7	614.4	1312	861.8	0	791.3	180.7	0	34.31	100	100	39.69	86.23
902	1006	2	1	+/+	Male	73	111565	2	70.8	142.9	0	60.6	118.2	370.6	291	295.4	0	151	66.8	0	-1.51	100	100	48.11	77.04
902	1006	2	1	+/+	Male	77	117321	8	48.7	49.8	0	34.6	78.6	538.5	1738.3	1712.9	0	930.1	325.2	0	1.46	100	100	46.49	81.29
902	1006	2	1	+/+	Male	77	117338	1	24.6	23.7	0	31.7	497.5	1420.5	1992.7	1677.8	0	1194.8	279.7	0	15.8	100	100	40.04	85.96
902	1006	2	1	+/+	Male	77	117348	3	25.6	16.5	0	19.7	45.8	348.6	466.8	350.7	0	104.5	42.9	0	24.87	100	100	77.61	90.81
902	1006	2	1	+/+	Male	77	127772	6	31.2	40.5	0	37	106	229.5	308.5	393.1	0	114.2	76.2	0	-27.42	100	100	62.98	75.3
902	1006	2	1	+/+	Male	78	127778	4	21.7	27	0	70.2	334.5	618.6	641.1	473.4	0	180.7	97.3	0	26.16	100	100	71.81	84.82
902	1006	2	1	+/+	Male	77	135163	1	23.2	21.3	0	24.1	284.6	2023	2686	2379.4	0	1543.1	832.1	0	11.41	100	100	42.55	69.02
902	1006	2	1	+/+	Male	76	135180	3	16.4	19.7	0	25.1	486.3	1173.8	1577.7	1745.7	0	929.2	282.7	0	-10.65	100	100	41.1	82.08
902	1006	2	1	+/+	Male	78	138630	5	51.1	62.5	0	38.9	115.2	976.7	1469.2	1429.2	0	701.6	168	0	2.72	100	100	52.25	88.57
902	1006	2	1	-/-	Male	73	111590	3	23.7	35.2	0	163.1	671.4	1753.9	1807.1	1256.9	0	823.3	272.6	0	30.45	100	100	54.44	84.92
902	1006	2	1	-/-	Male	73	111592	4	42.4	34.2	0	112.3	378.5	1088.9	1800.2	1794.9	0	902.8	175.8	0	0.29	100	100	49.85	90.23
902	1006	2	1	-/-	Male	77	117319	6	37.5	27.8	0	97.6	439.5	1367.7	1674.3	1670.8	0	437.6	122	0	0.21	100	100	73.86	92.71
902	1006	2	1	-/-	Male	77	117320	7	20.6	23.8	0	98.1	450.7	1840.5	2369.6	2639.2	0	1268.4	348.3	0	-11.38	100	100	46.47	85.3
902	1006	2	1	-/-	Male	77	117341	2	30.3	45.4	0	54.1	140.6	446.7	969.3	813.4	0	482.4	188.5	0	16.08	100	100	50.23	80.55
902	1006	2	1	-/-	Male	78	127734	3	35.8	50.3	0	79.1	381.4	1495	2250.3	1534.7	0	463.8	181.6	0	31.8	100	100	79.39	91.93
902	1006	2	1	-/-	Male	77	127771	5	19.7	22.6	0	55	458.9	1751.5	2493.1	2036.3	0	716.4	207.1	0	18.32	100	100	71.26	91.69
902	1006	2	1	-/-	Male	77	135164	2	16.8	19.8	0	42.4	403.3	1154.4	1883.7	1476.6	0	1282.2	702.1	0	21.61	100	100	31.93	62.73
902	1006	2	1	-/-	Male	76	135184	4	30.8	20.6	0	343.7	1198.3	1821.2	2315.9	1927.8	0	544.4	218.6	0	16.76	100	100	76.49	90.56



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	Average																								
	Highest Voltage											Prepulse Inhibition						Test					Working	ES Cell
station	P080	P085	P090	P100	P110	P120	PP080P120	PP085P120	PP090P120	PP100P120	PP090P110	PPI80/120	PPI85/120	PPI90/110	PPI90/120	PPI100/120	Validity	Release Flag	Test Date	Test Id	Scientist	Set	Line Order
	28.2	0	38	70.7	614.4	1312	881.8	0	791.3	180.7	0	34.31	100	100	39.69	86.23	V	T	12/20/2000	16536016	Unknown Unknown	DB2	1
	142.9	0	60.5	118.2	370.6	291	296.4	0	151	66.8	0	-1.51	100	100	48.11	77.04	V	T	12/20/2000	16536041	Unknown Unknown	DB2	1
	40.8	0	34.5	78.6	638.5	1738.3	1712.9	0	930.1	326.2	0	1.46	100	100	46.49	81.29	V	T	1/17/2001	16536065	Unknown Unknown	DB2	1
	23.7	0	31.7	407.5	1420.5	1992.7	1677.8	0	1194.8	279.7	0	15.8	100	100	40.04	85.96	V	T	1/17/2001	16536091	Unknown Unknown	DB2	1
	16.5	0	19.7	45.8	348.8	468.8	350.7	0	104.5	42.9	0	24.87	100	100	77.61	90.81	V	T	1/17/2001	16536116	Unknown Unknown	DB2	1
	40.5	0	37	106	229.5	308.5	393.1	0	114.2	76.2	0	-27.42	100	100	62.99	75.3	V	T	2/22/2001	16536141	Brenda Ramirez	DB2	1
	27	0	70.2	334.5	818.6	841.1	473.4	0	180.7	97.3	0	26.18	100	100	71.81	94.82	V	T	2/22/2001	16536166	Brenda Ramirez	DB2	1
	21.3	0	24.1	284.6	2023	2680	2379.4	0	1543.1	832.1	0	11.41	100	100	42.55	89.02	V	T	3/19/2001	16536191	Todd Westergard	DB2	1
	19.7	0	25.1	466.3	1173.8	1677.7	1745.7	0	929.2	282.7	0	-10.86	100	100	41.1	82.08	V	T	3/19/2001	16536216	Todd Westergard	DB2	1
	62.6	0	38.9	115.2	976.7	1469.2	1429.2	0	701.6	168	0	2.72	100	100	52.25	88.57	V	T	3/28/2001	16536241	Phu Tran	DB2	1
	35.2	0	153.1	671.4	1753.9	1807.1	1256.9	0	823.3	272.6	0	30.45	100	100	54.44	84.92	V	T	12/20/2000	16536266	Unknown Unknown	DB2	1
	34.2	0	112.3	378.5	1088.9	1800.2	1794.9	0	902.8	176.8	0	0.29	100	100	49.85	90.23	V	T	12/20/2000	16536291	Unknown Unknown	DB2	1
	27.8	0	97.6	439.6	1387.7	1674.3	1670.8	0	437.6	122	0	0.21	100	100	73.88	92.71	V	T	1/17/2001	16536316	Unknown Unknown	DB2	1
	23.8	0	98.1	460.7	1840.6	2389.6	2639.2	0	1268.4	348.3	0	-11.38	100	100	46.47	85.3	V	T	1/17/2001	16536341	Unknown Unknown	DB2	1
	46.4	0	64.1	140.8	446.7	969.3	813.4	0	492.4	188.6	0	16.08	100	100	60.23	80.65	V	T	1/17/2001	16536366	Unknown Unknown	DB2	1
	60.3	0	79.1	381.4	1495	2250.3	1534.7	0	463.8	181.6	0	31.8	100	100	79.39	91.93	V	T	2/22/2001	16536391	Brenda Ramirez	DB2	1
	22.6	0	65	468.9	1761.5	2493.1	2036.3	0	718.4	207.1	0	18.32	100	100	71.26	91.69	V	T	2/22/2001	16536416	Brenda Ramirez	DB2	1
	19.8	0	42.4	403.3	1154.4	1883.7	1478.8	0	1282.2	702.1	0	21.61	100	100	31.93	62.73	V	T	3/19/2001	16536441	Todd Westergard	DB2	1
	20.8	0	343.7	1198.3	1821.2	2316.9	1927.8	0	644.4	218.6	0	16.76	100	100	76.49	90.66	V	T	3/19/2001	16536466	Todd Westergard	DB2	1

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Gene	ES Cell Line	F #	N #	Age Bin	Genotype	Gender	Study Procedure Name	Observable	Statistic	Statistic Value	Mouse Count (n)
902	1006	2	1	49	-/-	Female	necropsy	liver weight	1-p value vs. WT controls	0.96	3
902	1006	2	1	49	-/-	Female	necropsy weights	liver weight	1-p value vs. WT controls	0.96	3
902	1006	2	1	90	-/-	Female	hematology	platelets	1-p value vs. WT controls	0.95	4
902	1006	2	1	90	-/-	Male	serum chemistry	triglycerides	1-p value vs. WT controls	0.99	3
902	1006	2	1	90	-/-	Male	serum chemistry	low density lipoprotein	1-p value vs. WT controls	0.99	3
902	1006	2	1	180	-/-	Male	hematology	absolute basophils	1-p value vs. WT controls	0.97	4
902	1006	2	1	180	-/-	Male	mouse metrics	body length	1-p value vs. WT controls	1	3
902	1006		1		-/-	Male	startle	P090, average	1-p value vs. WT controls	0.98	9
902	1006		1		-/-	Male	startle	P090, standard deviation	1-p value vs. WT controls	0.98	9
902	1006		1		-/-	Male	startle	P100, average	1-p value vs. WT controls	0.98	9
902	1006		1		-/-	Male	startle	P100, standard deviation	1-p value vs. WT controls	0.99	9
902	1006		1		-/-	Male	startle	P110, average	1-p value vs. WT controls	0.97	9
902	1006		1		-/-	Male	startle	P110, standard deviation	1-p value vs. WT controls	0.97	9
902	1006		1		-/-	Male	startle	P120, average	1-p value vs. WT controls	0.97	9
902	1006		1		-/-	Male	startle	P120, standard deviation	1-p value vs. WT controls	0.96	9